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Original Article

Incidence of Breast Cancer in Egyptian Females in Correlation to Different Mammographic ACR Densities

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Abstract

Introduction: The density of breast tissue, radiologically referred to as fibroglandular mammary tissue, was found to be a predisposing factor for breast cancer (BC). However, the stated degree of elevated BC risk varies widely in the literature.

Aim: The purpose of this study was to determine the relationship between different breast mammography densities and the risk of breast cancer in Egyptian women..

Patients and methods: An analytical cross-sectional prospective study was conducted at Ain Shams University Hospital and Private Centre between December 2020 and December 2021. The study included 814 asymptomatic females 40 years old or above, who came for BC screening using full-field digital mammography.

Results: The incidence of BC was found in 84 females (10.3%). Breast cancer incidence was 6.3% in females with ACR-A density, 8.5% in women with ACR-B density, 16.3% in women with ACR-C density, and 27.8% in women with ACR-D density (p<0.001). Using logistic regression analysis, we showed that three types of breast density increased the risk of BC, where patients with type B, type C, and type D breast density had a 1.39, 2.92, and 3.12 times more risk for BC, respectively (p=0.010, p=0.003, and p=0.036, respectively).

Conclusion: Among Egyptian females, the incidence of BC is 10.3%. Our data revealed that the greater the breast density, the higher the incidence of BC, and affirmed that breast density is a risk factor for BC development.

Keywords

breast cancer, breast density, mammography

INTRODUCTION

Breast cancer is a malignant tumor that originates in the cells of the breast tissue. It is the most common cancer in women worldwide, accounting for 24.2% of all cancer cases among women. According to the latest World Health Organization statistics, there were an estimated 2.3 million new cases of breast cancer in 2020; it is the second leading cause of cancer death in women after lung cancer. The risk of developing breast cancer increases with age, and most cases occur in women over the age of 50.[1]

The presence of breast cancer can be detected through various methods, including mammography, ultrasound, and magnetic resonance imaging (MRI). If breast cancer is suspected, a biopsy may be performed to remove a sample of tissue for further examination.[1]

The mortality rate of breast cancer varies depending on the stage at diagnosis and the availability of treatment.

According to the American Cancer Society, the 5-year relative survival rate for women with breast cancer is 90%. However, this rate drops significantly for women with advanced stage breast cancer.[2]

Recent statistics show that the incidence of breast cancer is increasing worldwide. This is thought to be due to a combination of factors, including increased awareness and screening, as well as changes in reproductive and lifestyle factors. However, mortality rates have been decreasing in many countries due to improvements in early detection and treatment.[2]

Despite these advances, breast cancer remains a significant public health concern. According to the WHO, there were an estimated 685,000 deaths from breast cancer worldwide in 2020. Continued research and investment in prevention, early detection, and treatment are essential to reducing the burden of this disease.[1,3]

A large Egyptian systematic review and meta-analysis revealed that BC was the most common cancer, accounting for 42% of all cancer cases in Egyptian females, with the majority presenting in advanced stages.[4]

The World Health Organization's principal objective is to reduce the BC-related burden and BC-related mortality which is suggested to be achieved by early detection and proper management of BC.[1]

BC screening contributes considerably to the early detection of asymptomatic cancer, which leads to less intrusive therapies and better outcomes since the disease is found before the progression of the tumor. The most effective imaging method that is still advised for all women to use for BC screening is mammography.[5]

Accordingly, a number of nations have put in place national programs for BC screening, wherein women undergo routine mammography screenings. Women between the ages of 50 and 69 are screened in the majority of nations since it is thought that they are the most suitable population to gain advantages from this screening.[6]

The density of breast tissue, radiologically referred to as fibroglandular mammary tissue, was found to be a risk factor for BC in the early twentieth century. It was reported that dense breasts were more likely to develop BC than fatty breasts.[6] However, the stated degree of elevated BC risk varies widely in the literature, from a one- to a six-fold greater risk.[5,8,9]

AIM

The present study aims to detect the relationship between different breast mammographic densities and the risk for BC in Egyptian females.

DESIGN

Analytical cross-sectional prospective study.

PATIENTS AND METHODS

Asymptomatic females who are 40 years of age or older and eligible for screening mammography were included in the study which was approved by the institutional Ethics Committee.

The study included 814 asymptomatic females who came for BC screening. After the study was approved by the Ethics Committee of the university, asymptomatic females of 40 years of age or older who were eligible for screening mammography were included into our study. Any female who was contraindicated for mammography was excluded, such as a pregnant female or a female under the age of 40, for whom ultrasound (US) is the preferred method.

All females were submitted to demographic and clinical data collection and imaging procedures using full-field digital mammography, a device developed by GE Healthcare (Senographe 2000 D full-field digital mammography Essential GE Healthcare). For all patients, two standard views medio-lateral-oblique (MLO) and cranio-caudal (CC) views were obtained.

Then, according to the Breast Imaging Reporting and Data Systems (BI-RADS) Atlas 5th Edition 2013[10], all females were classified into four density categories based on mammographic findings: excessively fatty (ACR-A), dispersed density (ACR-B), heterogeneous density (ACR-C), and extremely dense (ACR-D).

On the basis of the BI-RADS lexicon[10], females were classified as BI-RADs 0 (need additional evaluation), 1 (negative), 2 (benign), 4 (suspicious), and 5 (highly suggestive of malignancy). Patients with BI-RADs 0, 4, and 5 underwent complementary US using GE LOGIQ P6 XD clear (GE health, Chicago, USA), using a high-frequency linear probe (9-12 MHZ) to scan the entire breast and axilla using combined techniques (radial, axial, and longitudinal). Cases with BI-RADs 4 and 5 underwent US-guided biopsy. Patients with BI-RADs 0 were categorized to BI-RADS 3, 4, or 5 according to the result of complementary US.

Statistical analysis

The statistical software for social sciences, version 23.0 (SPSS Inc., Chicago, Illinois, USA), was used to analyze the recorded data. The ranges and mean ± standard deviation (SD) were displayed for the quantitative statistics. Additionally, percentages and numbers were used to present qualitative factors. To compare the qualitative data, the chi-square test was applied, and to determine the independence of breast density as a predisposing factor for BC, multiple logistic regression was used. The confidence interval was set to 95% and the margin of accepted error was agreed to be 5%. Accordingly, p-value <0.005 reflects significant results.

RESULTS

Among the 814 females, the age ranged from 40 to 79 years (mean age 53.78±10.22). Most of the females were between 40 to 50 years of age (323 females; 39.7%). According to the BI-RADS 5th edition, ACR-A density was found in 176 females (21.6%), ACR-B density in 424 females (52.1%), ACR-C density in 196 females (24.1%), and ACR-D density

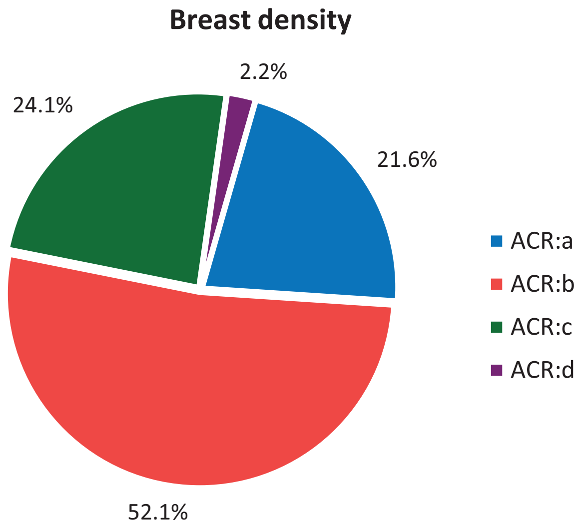


Figure 1. Pie chart breast density distribution among study group.

in 18 females (2.2%) **(Fig. 1)**.

The age of the females and the type of their breast density showed a statistically significant relation (p<0.001), where the oldest females were found to have breast density type A (64.34±5.83 years) and the youngest had breast density type D (43.33±4.51 years) **(Table 1)**.

The incidence of BC was found in 84 females (10.3%). The BC incidence in females with ACR-A was 6.3%, ACR-B was 8.5%, ACR-C was 16.3% **(Fig. 2)** and ACR-D was 27.8% **(Fig. 3)** (p<0.001) **(Table 2)**.

Fig. 2 illustrates the case of a 43-year-old woman who underwent routine breast cancer screening through both mammography and ultrasound imaging, revealing high breast density according to the American College of Radiology's classification system (ACR-D). **Figs 2A, 2B** display the mammography images obtained from this examination, with (A) showing a dense, irregular mass located in the upper outer quadrant (UOQ) region of the right breast that is most apparent when viewed from below (MLO position). This finding is further highlighted in **Fig. 2B**, where it appears as an irregular shape with indistinct margins. **Fig. 2C** displays an accompanying ultrasound image, which depicts a similarly shaped, but now hypoechoic and irregular mass situated within the same area. Based on these findings, the radiologist assigned a Bi-RADS assessment score of category 5, indicating a highly suspicious malignancy. Subsequent diagnostic confirmation via US-guided core needle biopsy performed outside the screening context uncovered a pathological diagnosis of invasive ductal carcinoma (IDC), classified as grade II based on histopathologic evaluation.

Fig. 3 depicts a 48-year-old woman who underwent regular breast cancer screenings. During her examinations, we observed elevated levels of dense tissue in her breasts, categorized by the American College of Radiology as type C. We employed mammography with complementary ultrasonography to visualize any potential abnormalities. **Fig. 3** showcase the results of our mammography scans taken during the craniocaudal (CC) and medial-lateral oblique (MLO), respectively, highlighting a partial yet undefined mass formation in the Rt upper inner quadrant (UOQ) zone. Compensatory ultrasound shows hypoechoic irreg-

Table 1. Relation between age of females and their type of breast density (n=814)

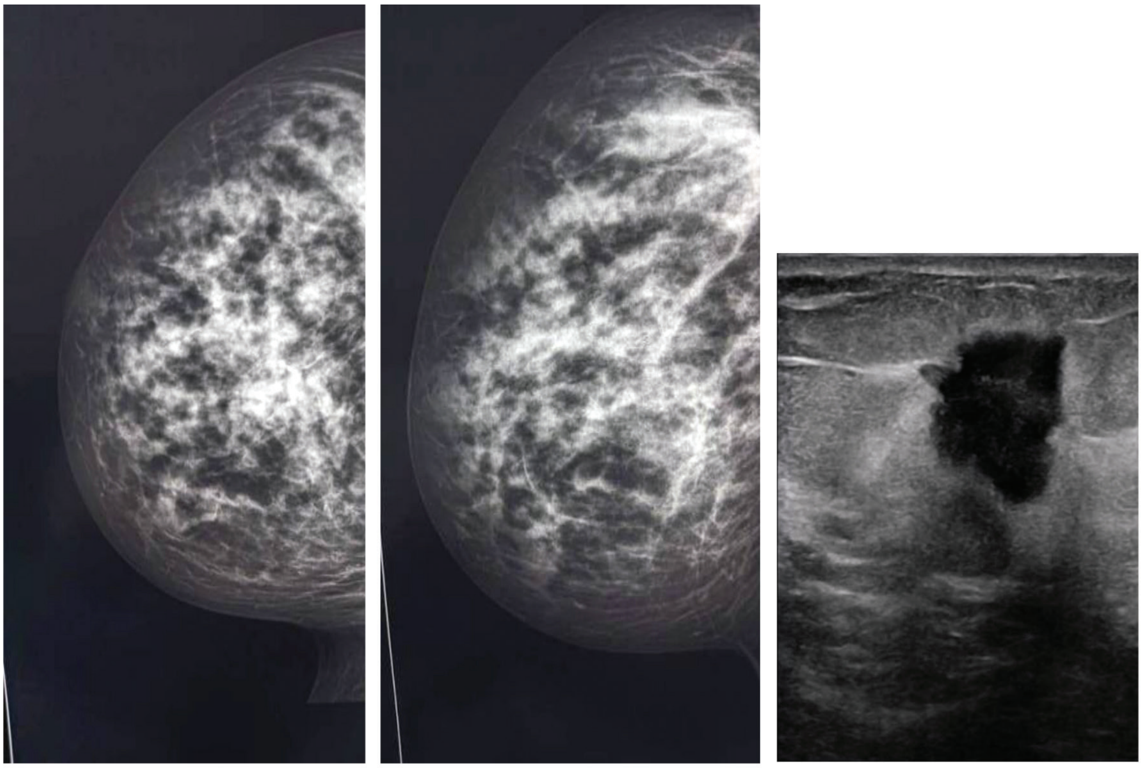
	Type A	Type B	Type C	Type D	*P*-value
Age (mean ± SD)	64.34±5.83)	53.18±7.95	45.02±3.72	43.33±4.51	<0.001* [a]

[a] Kruskal-Wallis test

Table 2. Association between breast density and BC among study groups (n=814)

Breast density	Breast cancer				Total	
	Negative		Positive			
	No.	%	No.	%	No.	%
ACR-A	165	93.8%	11	6.3%	176	100.0%
ACR-B	388	91.5%	36	8.5%	424	100.0%
ACR-C	164	83.7%	32	16.3%	196	100.0%
ACR-D	13	72.2%	5	27.8%	18	100.0%
Total	730	89.7%	84	10.3%	814	100.0%
Chi-square test	18.252					
p-value	<0.001**					

χ^2: chi-square test for number (%). ***p*-value <0.001 is highly significant



A B C

Figure 2. Detection of highly suspicious mass lesions in a patient with ACR-C breast density using mammography and ultrasound imaging biopsy revealed IDC-II.

ular mass and ultrasound guided biopsy taken with pathology revealed IDC-II.

As risk factors for BC, three types of breast densities increased the risk of BC, where females with type B breast density had 1.39 times more risk of breast cancer, while type C patients had 2.92 times more risk, and finally, type D females had 3.12 times more risk for breast cancer (p=0.010, p=0.003, and p=0.036, respectively) **(Table 3)**.

DISCUSSION

Currently, the most widely used tool available for clinically categorizing mammographic density is the BI-RADS, which was released in 2013. Four types of breast density are defined by this system: excessively fatty (ACR-A), dispersed density (ACR-B), heterogeneous density (ACR-C), and highly dense (ACR-D).[10] Using BI-RADS 5th edition, we aimed in our study to find the relationship between different breast mammographic densities and risk for BC in Egyptian females.

Table 3. Logistic regression for the breast density for BC among the study groups (n=814)

Characteristics	OR[a]	CI	*P* value
Type-A	0.54	1.740 – 19.125	0.068
Type-B	1.39	1.399 – 12.286	0.010*
Type-C	2.92	1.323 – 3.410	0.003*
Type-D	3.12	0.169 – 1.522	0.036*

[a] Multiple logistic regression

In this work, according to the BI-RADS 5th edition, among women who were screened for BC, group ACR-B is the most common type which was consistent with previous works.[9,11] We found that more than half of the females were categorized as ACR-B (52.1%), followed by ACR-C (24.1%), ACR-A (21.6%), and ACR-D (2.2%).

This was also similar to a previous Egyptian study by Ali and Raafat[12] which included 49,409 women who presented for screening mammography. The study showed that the majority of Egyptian females were categorized as ACR-B (49%), followed by ACR-C, ACR-A, and ACR-D, representing 49%, 25%, 23%, and 3%, respectively based on the BI-RADS.[12]

In another Egyptian study by Ahmed et al. that included 40 women with confirmed BC, based on the BI-RADS 5th edition, more than half of females were categorized as ACR-B (52.5%), followed by ACR-C (30%), ACR-A (15%), and ACR-D (2.5%).[13]

We found an inverse significant relationship regarding the age of the females and the type of their breast density (p<0.001), where the oldest females were found to have breast density type A (64.34±5.83 years) and the youngest had breast density type D (43.33±4.51 years). These results agreed with Al-Mousa et al., who concluded that increased

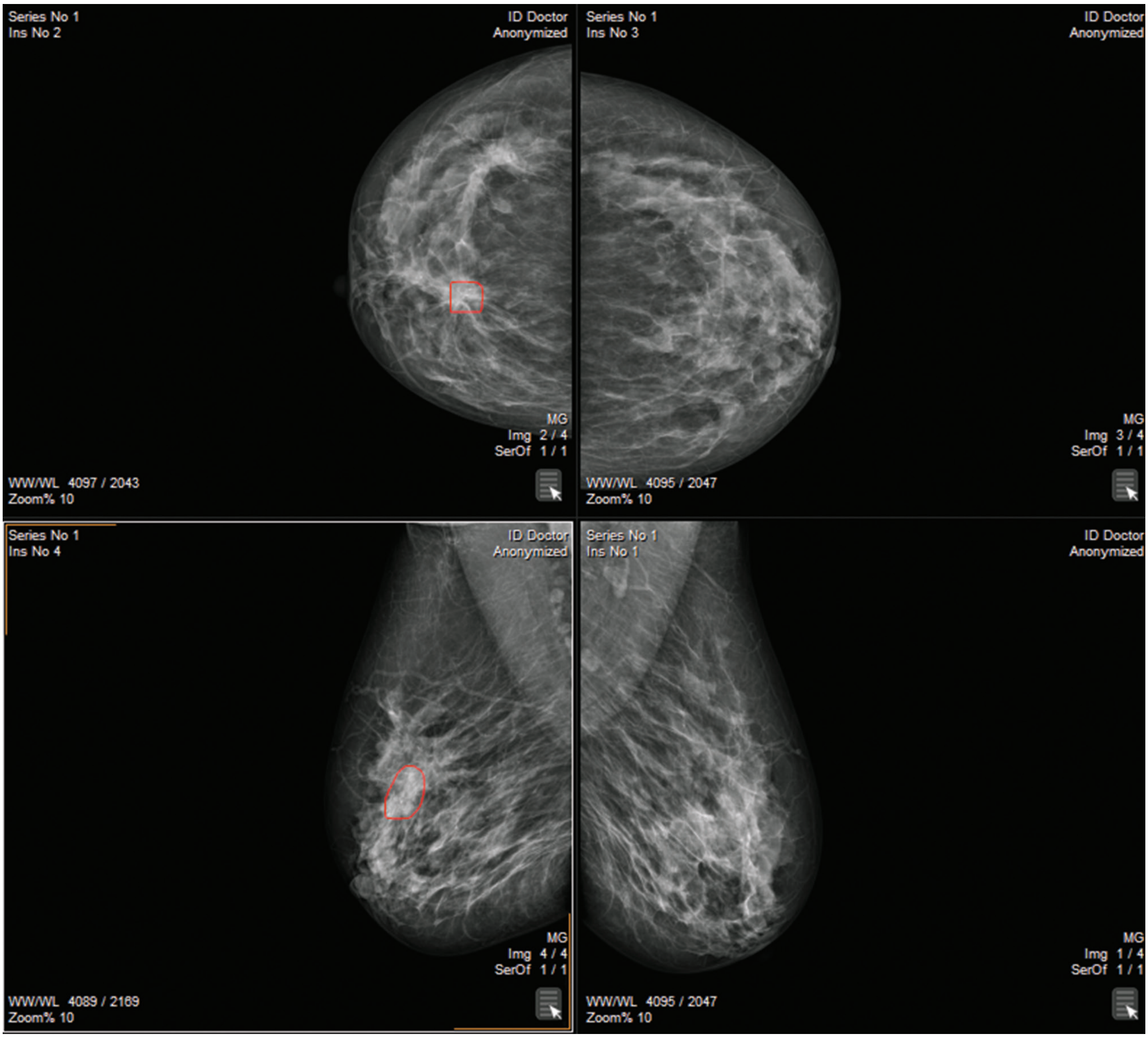


Figure 3. IDC III in a female undergoing routine breast cancer screening with increased dense tissue (ACR-C Type) visualized through mammography images.

breast density on mammography was inversely related to age.[14]

Likewise, Checka et al. observed a significant inverse relation between female ages and mammographically determined breast density (p<0.001); however, they added that age was not a reliable indicator of breast density as they observed a significant percentage of postmenopausal women still having dense breasts on mammography.[15]

These results contradict the fact that BC is more frequent among older females and in dense breasts. However, this may be explained by the low mammographic sensitivity in young women with more dense breasts[16] which may obscure the early detection of BC among young females which delays the presenting age. This emphasizes the need for individual-based screening program taking into consideration females' ages and breast densities.

In the present study, the incidence of BC among our population was found in 84 females (10.3%). This was higher than that reported in a recent Egyptian study performed by Ali and Raafat, who found that among 49,409 women presented for screening mammography 1500 had BC representing only 3%.[12] Different sample sizes may be the cause for this variation.

The BC incidence in females with ACR-A was 6.3%, ACR-B was 8.5%, ACR-C was 16.3%, and ACR-D was 27.8% (p<0.001), indicating a significant relation between the incidence of BC and breast density, in which the females with extremely dense breasts (ACR-D) are more susceptible to develop BC. This result was confirmed by logistic regression analysis which showed that three types of breast densities increased the risk of BC, where patients with type B, type C, and type D breast density had a 1.39, 2.92, and 3.12 times more risk for BC, respectively (p=0.010, p=0.003, and p=0.036, respectively). These findings settle breast density as a predisposing factor for BC development, showing that the greater the breast density, the higher the incidence of BC.

Our findings support the results of many previous studies. Cohort studies have shown a significant correlation between increasing breast mammographic density and the increased incidence of BC in women.[7,12,17]

As mentioned in our study, Ali and Raafat showed that the incidence of BC in females with ACR-D (13.7%) was the highest followed by that in females with ACR-C (3.3%), ACR-B (2.7%), and ACR-A (2.2%).[12]

It was demonstrated by Ahmadinjad et al. that BC growth was more likely to occur in breasts with high densities, more than in breasts with low densities (p=0.007).[18]

Contrary to our findings, Ahmed et al. reported no relation between BC and breast density in a study conducted on a total of 40 females who were radiologically and histopathologically diagnosed with BC. The authors found that the percentage of cases with BC was the highest among females with intermediate breast density (ACR-B), then increased with ACR-C and ACR-A, respectively, suggesting that dense breast tissue should not be regarded as a risk factor for BC.[13]

Also, Kamal et al. studied the role of breast density as one of the BC risk factors in accordance with menopausal status. In contrast to our findings, they reported that in premenopausal women, breast density was insignificantly related to BC, whereas breast density showed an inverse significant relationship to BC in postmenopausal women. After a logistic regression analysis, Kamal et al. found that decreased breast density is a significant independent predisposing factor for BC (p=0.009).[19]

This discrepancy may be related to some factors, including variations in the breast density assessment technique, adjustments made during the analyses, and, to some extent, variations in the demographics of the population being studied, such as menopausal status, ethnicity, and lifestyle variations; however, these reasons are still debatable.

The fact that our study is prospective in design and conducted at one of the largest Egyptian centers for BC screening strengthens our work. However, our study is limited by the relatively small sample size from a single Egyptian center, accordingly, a larger multicentric study is needed to be more representative of the Egyptian female population. Additionally, the study sample was not evenly distributed throughout the ACR and age groups, which might have skewed the findings. Furthermore, the study did not include other parameters that are proposed to be linked to an increased risk of breast density and BC in the past, such as parity, menopausal status, and hormonal use.

We acknowledge that these factors should be included in future research. Finally, we did not report the clinical-histopathological data as it was away from our aim.

CONCLUSION

Among Egyptian females, the incidence of BC is 10.3%. Females with extremely dense breasts (ACR-D) are more susceptible to developing BC. Overall, our data showed that the greater the breast density, the higher the incidence of BC, and affirmed that breast density is a risk factor for BC development. We recommended a nationwide comprehensive program for BC screening in the whole of Egypt not only for the major government and private hospitals and in screening programs, but breast density estimation should also be considered as a tool in BC prediction.

Conflict of interest

None.

Availability of data and materials

Available on request.

Consent for publication

All authors have approved the manuscript for submission.

Funding

None.

Author contributions

M.R.H.S.: conceptualization, methodology, data collection, data analysis, manuscript writing; N.A.T.C.: methodology, data collection, data analysis, manuscript writing; A.A.B.M.: data collection, data analysis, manuscript writing; G.E.E.Y.: methodology, data collection, manuscript.

Ethical considerations

The study took place at Ain Shams University Hospital and Private Centre in the period from December 2020 to December 2021 after obtaining the preliminary approval of the study protocol and the completion of case collection. The study outcomes were approved by the local Ethics Committee with code FMASU M D 236/2020.

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Заболеваемость раком молочной железы у египетских женщин в зависимости от различной плотности маммографических ACR

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Резюме

Введение: Плотность молочной железы, радиологически называемая фиброзно-железистой тканью молочной железы, оказалась предрасполагающим фактором развития рака молочной железы (РМЖ). Однако заявленная степень повышенного риска РМЖ широко варьируется в литературе.

Цель: Найти взаимосвязь между различной плотностью маммографии молочной железы и риском рака молочной железы у египетских женщин.

Пациенты и методы: Аналитическое поперечное проспективное исследование было проведено в университетской больнице и частном центре Айн-Шамс в период с декабря 2020 по декабрь 2021 года. В исследование были включены 814 бессимптомных женщин в возрасте 40 лет и старше, пришедших на скрининг РМЖ с использованием полноформатной цифровой маммографии.

Результаты: Заболеваемость РМЖ выявлена у 84 женщин (10.3 %). Заболеваемость РМЖ у женщин с ACR-A составила 6.3 %, ACR-B - 8.5 %, ACR-C - 16.3 % и ACR-D - 27.8 % со значением $p<0.001$. Используя анализ логистической регрессии, мы показали, что три типа плотности груди увеличивают риск РМЖ, при этом пациентки с плотностью груди типа B, типа C и типа D имели риск развития РМЖ в 1.39, 2.92 и 3.12 раза соответственно ($p=0.010$, $p=0.003$ и $p=0.036$ соответственно).

Заключение: Среди египетских женщин заболеваемость РМЖ составляет 10.3 %. Наши данные показали, что чем больше плотность молочной железы, тем выше заболеваемость РМЖ, и подтвердили, что плотность молочной железы является фактором риска развития РМЖ.

Ключевые слова

рак молочной железы, плотность молочной железы, маммография